

### **REMARKS**

Reconsideration is respectfully requested. Claims 60-69 are pending. Claims 1-59 have been canceled.

With respect to all amendments and cancelled claims, Applicants have not dedicated or abandoned any unclaimed subject matter and moreover have not acquiesced to any rejections and/or objections made by the Patent Office. Applicants reserve the right to pursue prosecution of any presently excluded claim embodiments in future continuation and/or divisional applications.

#### **Claim Rejection Under 35 U.S.C. § 103**

Claims 60-69 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Kayyem et al. (WO 98/20162) (“*Kayyem*”), in view of Shuber (US 5,633,134) (“*Shuber*”). Applicants respectfully traverse.

To establish a *prima facie* case the prior art reference(s) must teach or suggest each and every limitation of the rejected claims. *In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991); M.P.E.P. §2142.

Claims 61-69 depend from claim 60, which requires a first probe and second probe that are “substantially complementary to said first domain,” but that have different nucleotides at the “interrogation position.” Thus, claim 60 not only requires that two probes compete for hybridization to the same domain, but also requires that the two probes have different nucleotides at the interrogation position that could be “perfectly complementary” to the same “detection position” in the first domain of the target sequence.

The instant application also discloses that “detection position” is on the target sequence, and: [D]etection position is a single nucleotide... [or] may comprises a plurality of nucleotides, either contiguous with each other or separated by one or more nucleotides. Page 12, lines 9-13.

The instant application further discloses that “interrogation position” is “the base which basepairs with the detection position in a hybrid.” Page 12, lines 13-14. Thus, the “interrogation position” is in the probe.

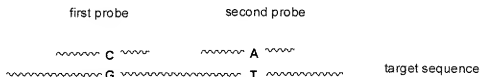
The Examiner states in the Office Action that:

Shuber is relied on for teaching multiple oligonucleotide probes specific for one domain. Shuber teach [sic] multiple oligonucleotide probes with labels for determining nucleotides at the detection position at col. 5 lines 13-21. Here Shuber describes ASOs (labeled probes) which are used to detect mutations at multiple interrogation positions.

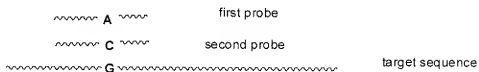
Therefore, the Examiner concedes that *Shuber* only discloses probes that are used to detect mutations at multiple detection positions (referred to as “interrogation positions” by the Examiner) in the

target sequence. Corresponding to the different detection positions in the target sequence there are different positions in each probe, and they are not the same "interrogation position" as claim 60 requires. This can be further illustrated in the following drawing by comparing to the requirement of claim 60 (the illustration herein is by no means to be interpreted as adding limitation to claim 60):

### Shuber



### Claim 60



As the Examiner can appreciate, the "interrogation positions" referred to by the Examiner are positions in the target sequence. Therefore, *Shuber* is directed to detection of multiple detection positions in the target sequence (here in the drawing are the positions in the target sequence that have a G and a T). The detection is accomplished by using multiple ASOs, each is complementary to different detection positions (here in the drawings are the first probe and second probe, each has a C or an A to basepair with the G and the T of the detection positions in the target sequence, respectively).

Therefore, the multiple probes of *Shuber* are not, as claimed here, complementary to the same detection position. Instead, the multiple probes of *Shuber* are each complementary to different detection positions on the target sequence.

In contrast, also as illustrated in the drawing and for illustrative purposes only, one embodiment of claim 60 requires one detection position in the target sequence, here is the position with a G. There are two probes, the first and second, each has different base in the same interrogation position corresponding to the detection position: one probe, here the second probe, has a C in the interrogation position, which is a perfect match with the G in the detection position of the target sequence; the other probe, here the first probe, has an A in the interrogation position, which is a mismatch with the G in the detection position of the target sequence. Thus, the presence of the second probe indicates it is a G in the detection position of the target sequence.

The Examiner also states in the Advisory Action that "there is also no limitation in the claim which requires the interrogation position to be identical." Applicants respectfully disagree.

Claim 60 recites "an interrogation position" in line 9, and refers it later in lines 12 and 14 as "said interrogation position." Thus, what is recited in claim 60 is the same interrogation position.

For the forgoing reasons, *Shuber* does not disclose two or more probes have different nucleotides at the interrogation position that could be "perfectly complementary" to the same "detection position" in the first domain of the target sequence.

*Kayyem* does not expressly teach or suggest what *Shuber* lacks. *Kayyem* discloses a probe that hybridizes to two domains on two different sequences - one is on the anchor sequence and the other is on the target sequence, and two probes hybridize to two different domains of the target sequence. As demonstrated above, *Shuber* only discloses multiple probes hybridized to different detection positions of the target gene. *Kayyem* and *Shuber* thus fail to teach, alone or in combination, a first probe and a second probe "substantially complementary to said first domain," their difference being different nucleotides at the same "interrogation position" as required by claim 60.

Because *Kayyem* and *Shuber* taken together do not teach all of the elements of independent claim 60, and of claims 61-69 dependent thereon, claims 60-69 is nonobvious over *Kayyem* in view of *Shuber*. Accordingly, Applicants respectfully request that the rejection be withdrawn.

### CONCLUSION

Applicants respectfully submit that the claims are now in condition for allowance and early notification to that effect is respectfully requested. If the Examiner feels there are further unresolved issues, the Examiner is respectfully requested to phone the undersigned at (415) 442-1000.

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